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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s): Jeffrey R. Sampson et al.

Serial No.: 09/836,012

Examiner: Chunduru, Suryaprabha

Filing Date: April 17, 2001

Group Art Unit: 1637

Title: Method and Reagents for Analyzing the Nucleotide Sequence of Nucleic Acids

COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria VA 22313-1450

TRANSMITTAL OF REPLY BRIEF

Sir:

Transmitted herewith is the Reply Brief with respect to the Examiner's Answer mailed on  
This Reply Brief is being filed pursuant to 37 CFR 1.193(b) within two months of the date of the Examiner's  
Answer.

(Note: Extensions of time are not allowed under 37 CFR 1.136(a))

(Note: Failure to file a Reply Brief will result in dismissal of the Appeal as to the claims made subject to an expressly  
stated new grounds of rejection.)

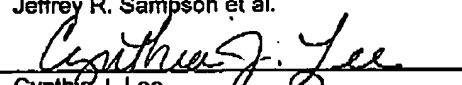
No fee is required for filing of this Reply Brief.

If any fees are required please charge Deposit Account 50-1078.

Respectfully submitted,

Jeffrey R. Sampson et al.

By

  
Cynthia J. Lee  
Attorney/Agent for Applicant(s)

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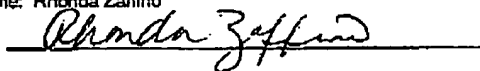
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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
BOARD OF PATENT APPEALS AND INTERFERENCES**

In Re Application of:

**Jeffrey R. Sampson *et al.***

Serial No.: **09/836,012**

Filed: **April 17, 2001**

For: **Method and Reagents for Analyzing  
the Nucleotide Sequence of Nucleic Acids**

Confirmation No.: **6991**

Group Art Unit: **1637**

Examiner: **Chunduru, Suryaprabha**

Docket No.: **10992153-1  
(50113-1220)**

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**REPLY TO EXAMINER'S ANSWER**

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Alexandria, Virginia 22313-1450

Sir:

The Examiner's Answer mailed April 4, 2006 has been carefully considered. In response thereto, please consider the following remarks.

***AUTHORIZATION TO DEBIT ACCOUNT***

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to deposit account no. 50-1078.

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### REMARKS

The Examiner has provided in the Examiner's Answer various responses to arguments contained in Applicants' Appeal Brief. In general, Applicants disagree with the position taken by the Examiner in the Examiner's Answer. In this regard, Applicants rely upon the arguments advanced in the Appeal Brief previously filed. However, Applicants offer the following additional comments in reply to the Examiner's Answer. Applicants note for the record that to the extent that every argument presented in Applicants' Appeal Brief that was not addressed in the Examiner's Answer, Applicants incorporate each of those arguments by reference into the present Reply Brief.

#### A. Reply to Examiner's Rejection based on *Southern et al.* in view of *Sorge*

Applicants continue to fundamentally disagree with the Examiner's position that the cited references, WO Patent No. 95/04160 issued to *Southern et al.* in view of U.S. Patent No. 6,607,878 issued to *Sorge* render claims 1-17 and 74-83 obvious. In addition to the remarks set forth in Applicants' Appeal Brief, Applicants offer the following additional comments, which they hope will be useful to the Board.

First, the Examiner admits on page 8, last paragraph of the Examiner's Answer that *Southern* teaches a "ladder tag" design. In this design, each discrete oligonucleotide sequence within the mixture is associated with a "spectrum" of mass entities. In contrast, each of the X-mer precursors of the independent claims possesses a single mass. Therefore, *Southern* does not teach or suggest the feature for which it is being offered.

Second, in response to Applicant's arguments that *Southern* does not teach or suggest a mixture or set of set of sub-mixtures as required by the independent claims, the Examiner stated that "[t]he limitation upon which [Applicants'] arguments are based, are not present in the

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claims.” *Examiner’s Answer* at 9. Applicants submit that the features do not have to be specifically recited in the claims. When an applicant chooses to be its own lexicographer and specifically defines claim terms in the specification, then the claims are to be compared to the prior art based on the defined claim terms. The definitions themselves need not be specifically recited in the claims. In the instant case, each of Applicant’s independent claims recites that “the mixture has a minimum mixture coverage complexity of at least  $56/N$ ...” The specification states: “The phrase ‘mixture coverage complexity’ ( $CC_M(\Omega)$ ) refers to the sum of the coverage complexities of each of the oligonucleotide precursors in the mixture and may be mathematically expressed as:

$$CC_M(\Omega) = \sum CC_O(\omega)''$$

*Specification* at page 22. Further, the specification states: “The phrase “oligonucleotide coverage complexity”  $CC_O(\omega)$  may be expressed mathematically as:

$$CC_O(\omega) = 1/4^L \prod_{i=1}^L S_{bp}(b_i)$$

where  $L$  is the number of nucleotide bases in the oligonucleotide precursor and  $b_i$  represents the  $i$ ’th unit of the oligonucleotide precursor.” *Id.* Simply according these claim terms their definition in the specification does not amount to reading limitations from the specification into the claims. Therefore, Applicants submit that, as Applicants define the claim terms in the specification, *Southern* in view of *Sorge* does not teach or suggest the following features of the independent claims, contrary to the Examiner’s assertion:

the mixture has a minimum mixture coverage complexity of at least  $56/N$  or wherein the set of sub-mixtures has a composite mixture coverage complexity of at least  $56/N$ , wherein  $N$  represents the number of distinct X-mer precursors in the mixture...

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any given oligonucleotide sequence in the mixture is attached to preferably a single tag with a discrete molecular weight.

(emphasis added).

Third, the Examiner asserts that:

the mass tags taught by Sorge et al. does represent 4096 different primer combinations in each pool, wherein each oligonucleotide also differs in sequence thus the over all molecular mass of each primer depends on the sequence of the oligonucleotide + the mass tag used, giving rise to a discrete molecular mass of any given oligonucleotide in the pool.

*Examiner's Answer* at 9-10. Applicants disagree. The Examiner offers no citation to the portion of *Sorge* that is supposed to teach or suggest this. Tags with different molecular mass that are "blocks of colors" or are used in "groups in multiples of fours" in order to be effective, as disclosed by *Sorge*, do not render obvious tags with discrete molecular weight, as recited in independent claims. These are different tags, the tags of the claims of which are non-obvious in view of *Sorge*.

Fourth, the Examiner asserts that:

an ordinary artisan would have a reasonable expectation of success that inclusion of discrete molecular weight tags would result in enriching sequence information of any oligonucleotide of interest....

*Examiner's Answer* at 9-10. Applicants disagree. If the Examiner is taking official notice of various claim limitations as being "well-known," then Applicant traverses the Examiner's assertion of official notice of these features of the claims.

In particular, Applicants traverse the assertion that features of the claims "would be obvious over the cited art in the absence of secondary considerations." *Id.* Applicants submit that the Examiner is taking statements from Applicants' own specification to arrive at the conclusion that this feature of Applicants' invention would be obvious based on the combination of references. For example, the instant Detailed Description section states the following:

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To enhance the versatility of the subject invention, the reagents can be provided in packaged combination, in the same or separate containers, so that the ratio of the reagents provides for substantial optimization of the method. The reagents may each be in separate containers or various reagents can be combined in one or more containers depending on the crossreactivity and stability of the reagents.

*Specification* at 65. Applicants submit this is impermissible hindsight reconstruction and that the Examiner has provided no documentary evidence in the prior art as to how it would be obvious to provide the kits and enzymes of the cited claims, in combination with the other features/steps of the claims.

For at least the foregoing reasons, *Southern* in combination with *Sorge* does not render the present claims obvious.

**B. Reply to Examiner's Rejection based on *Brenner* in view of *Sorge***

Applicants continue to fundamentally disagree with the Examiner's position that the cited references, U.S. Patent No. 5,654,413 issued to *Brenner* in view of U.S. Patent No. 6,607,878 issued to *Sorge* render claims 1, 3-6, and 74-80 obvious. In addition to the remarks set forth in Applicants' Appeal Brief, Applicants offer the following additional comments, which they hope will be useful to the Board.

The Examiner states that:

the claims do not exclude oligonucleotide tag as X-mer precursors because the tag definition clearly excludes the oligonucleotide sequence tags as a tag in their own lexicographer terminology, and the oligonucleotide sequence tags taught by *Brenner* are within the scope of X-mer precursors and note that the prior art terms are within the scope of the defined terms and thus the oligonucleotide tags are within the scope of the X-mer precursors.

*Examiner's Answer* at 11. The Examiner's statement is confusing, but based on Applicants' interpretation of the foregoing, Applicants disagree. Even if *Brenner* did not specifically define

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the term “tag” to exclude X-mer precursors, the independent claims recite “wherein each tag is covalently linked to at least one X-mer precursor” (emphasis added), thus specifically reciting that the X-mer precursor and the tag are not one and the same species. In that the Examiner continues to utilize the “tag” of *Brenner* to attempt to render obvious the “X-mer precursor” of the claims, Applicants traverse. For at least the foregoing reasons, *Brenner* in combination with *Sorge* does not render the present claims obvious.

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**CONCLUSION**

In summary, it is Applicants' position that Applicants' claims are patentable over the applied prior art references and that the rejection of these claims should be withdrawn. Appellant therefore respectfully requests that the Board of Appeals overturn the Examiner's rejection and allow Applicants' pending claims.

Respectfully submitted,

  
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